

FDA Presentation To PCNS

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EFFECT OF GHB ON MEASURES OF DAYTIME SLEEPINESS IN NARCOLEPSY

MEASURES OF DAYTIME SLEEPINESS IN GHB TRIALS

OMC-GHB-2

- Epworth Sleepiness Scale (Secondary)
- Frequency Of Sleep Attacks (Secondary)
- Duration Of Sleep Attacks (Secondary)

Scrima Study

- Sleepiness Index Of Multiple Sleep Latency Test (Primary)
- Frequency Of Sleep Attacks (Secondary)

Lammers Study

- Frequency Of Sleep Attacks (Secondary)
- Duration Of Sleep Attacks (Secondary)

OMC-SXB-21

None

Total Number Of Secondary Efficacy Measures In GHB Trials

OMC-GHB-2: 10

Scrima: 17

Lammers: 7

OMC-SXB-21: 0

OMC-GHB-2: Analysis Of Measures Of Daytime Sleepiness

Parameters	Treatment	Change in medians from baseline to endpoint	P-value for overall comparison *	P-value GHB group vs placebo
Excessive Daytime Sleepiness (Epworth Scale)	Placebo	-2.0	0.0006	
	3 g	-1.0		0.1137
	6 g	-3.5		0.1860
	9 g	-5.0		0.0001
Frequency of Daytime Sleep Attacks	Placebo	-0.26	0.0101	
	3 g	-0.20		0.1022
	6 g	-0.48		0.0497
	9 g	-0.48		0.0122
Duration of Daytime Sleep Attacks	Placebo	-3.10	0.0282	
	3 g	-5.00		0.9995
	6 g	-9.75		0.4413
	9 g	-7.95		0.0689

* based on ANCOVA

SCRIMA STUDY: ANALYSIS OF MEASURES OF DAYTIME SLEEPINESS

Sleepiness Index Of Multiple Sleep Latency Test

Treatment Group	GHB N = 20	Placebo N = 20
Mean Baseline Sleepiness Index	88.5	
Mean Overall Sleepiness Index During Treatment	87.2	90.3
Mean Overall Change From Baseline During Treatment	-1.3	1.8
GHB-Placebo Difference For Overall Treatment Effect	-3.1	
P-value for overall GHB-placebo difference	0.085	

SCRIMA STUDY: ANALYSIS OF MEASURES OF DAYTIME SLEEPINESS

Frequency Of Daytime Sleep Attacks (Attacks/Day)

Treatment Group	GHB N = 20	Placebo N = 20
Mean Baseline Frequency Of Sleep Attacks	2.8	
Mean Overall Frequency Of Sleep Attacks During Treatment	1.9	2.1
Mean Overall Change From Baseline During Treatment	-0.9	-0.7
GHB-Placebo Difference For Overall Treatment Effect	-0.2	
P-value for overall GHB-placebo difference	0.530	

LAMMERS STUDY: ANALYSIS OF MEASURES OF DAYTIME SLEEPINESS

Measure	Treatment Group	Median/Mean of Daily Score *			p-value for Change from Baseline to Endpoint (GHB vs placebo)
		Baseline	Endpoint	Baseline-Endpoint Change	
Severity of Daytime Sleepiness (n =24)	Placebo	1.60	1.59	-0.01	0.034
	GHB	1.60	1.28	-0.32	(Wilcoxon)
Frequency Of Daytime Sleep Attacks (n =24)	Placebo	1.83	2.14	0.31	0.0008
	GHB	2.17	1.36	-0.81	(ANCOVA*)

*Not a protocol-specified analysis

PROBLEMS WITH PROPOSED CLAIM FOR EXCESSIVE DAYTIME SLEEPINESS

- Most measures for excessive daytime sleepiness were secondary
- Only measure that was primary was “negative”
- Majority of measures “negative” (after adjustment of Type I error for multiple comparisons)
- Effects inconsistent across studies
- Lack of replication of positive results on any specific measure